OBSTRUCTIVE BILIARY CIRRHOSIS.

By William W. Ford, M.D., D.P.H.,
FELLOW IN PATHOLOGY, MCGILL UNIVERSITY, MONTREAL.

(*From the Molson Pathological Laboratory of McGill University.*)

The recent occurrence in Montreal of a case of cirrhosis of the liver which seemed to stand in etiological relationship to the pressure on the common bile-duct of an enlarged gland at the hilus of the liver, the autopsy material from this case being studied at the Royal Victoria Hospital, has led to a review of the literature of cirrhosis of the liver, with special reference to the frequency of this variety.

Although it has been recognized for many years that long-continued obstruction of the bile-ducts might cause an increase of the fibrous tissue of the liver, yet obstructive biliary cirrhosis was only established as a distinct pathological condition in 1874 and in 1876 by the labors of J. Wickham Legg, of London, and J. M. Charcot, of Paris. It was due to the observations of these men more than to any other investigations that light was thrown on the confused classification of morbid conditions of the liver, and it is to their great renown that they combined pathological, clinical, and experimental evidence in favor of their views. In vol. ix. of the *St. Bartholomew's Hospital Reports*, published in 1873, there appeared Wickham Legg's first experimental observation in this field, under the title of "On the Changes in the Liver which follow Ligature of the Bile-ducts." Legg tied the common bile-duct, necessarily without antiseptic precautions, in sixteen cats, twelve of which were left for a sufficient time to obtain characteristic changes in the liver. By these experiments he produced a well-marked jaundice, great emaciation, and finally death of the animals on which he had operated, and found at autopsy an enlargement of the liver, a distinct increase of the interlobular connective tissue, and an atrophy of the liver cells.

It may be noted that a similar result had been obtained experimentally by Oscar Wyss in 1866 and by Heinrich Mayer in 1872. Legg's first clinical observations were published in the *Transactions of the Pathological Society of London*, 1874 (vol. xxv., pp. 133 and 155). He here reports two cases. In the first case, an unmarried woman, aged twenty-three years, who during her short life had been highly intemperate, and who had shown for some two weeks before death marked jaundice, at autopsy was found to have a gallstone in the common duct, a dilatation of all the bile passages, and an interlobular cirrhosis of the liver. The second case was that of a man, aged thirty-five years, with a history of strict temperance, who had been jaundiced nine months and had an outbreak of xanthelasma multiplex on his face. At post-mortem hydatids of the liver, omentum, and recto-vesico pouch were found, with a resulting compression of the hepatic duct and an increase of the connective tissue about the portal canals. There was no other evidence of cirrhosis of the liver, and the obstruction of the hepatic duct was not complete.

In 1876, however, Legg published a case of congenital deficiency of the common bile-duct, the cystic and hepatic ducts opening in a blind sac, in which there was a well-marked interlobular and intralobular cirrhosis of the liver. In the same article he reviews the literature of congenital deficiency of the bile-ducts, and concludes that there is in all cases a cirrhosis of the liver dependent on the diseased condition of the ducts.

In the same year there appeared in the *Archives de Physiologie* Charcot and Gombault's well-known monograph on the diseases of the liver. These observers adopt an elaborate classification of the cirrhosis of this organ, in which classification, unfortunately, the terms used (annulaire, insular, and monolobulaire) are not always capable of proper interpretation. They recognize Hanot's cirrhosis, or hypertrophic cirrhosis with jaundice; Laennec's atrophic cirrhosis, and the cirrhosis dependent on obstruction of the biliary passages, the latter being anatomically identical with Hanot's cirrhosis. In the same monograph are reported four cases of cirrhosis of the liver following obstruction of the bile-ducts, the obstruction being caused by gallstones in the gall-bladder, by gallstones in the ampulla of Vater, cancer of the head of the pancreas, and angiocholitis of the larger bile passages. The anatomical picture of the livers of these cases is the same as that seen in Hanot's cirrhosis.

On the experimental side, Charcot reported observations on seven rabbits, in which he ligated the common bile-duct, producing jaundice and emaciation during life, and finding after death an enlargement of the liver, dilatation of all the bile passages, an interlobular cirrhosis, and many changes in the epithelium of the bile canaliculi. Charcot naturally operated without strict asepsis, and the presence of many leucocytes and small abscesses in various parts of the liver is a proof that he caused a serious infection of this organ; the question is thus raised whether the fibrous changes he saw in the livers of these rabbits were due simply to the damming back of bile in the dilated ducts, and its subsequent action on the liver cells, or to the growth of micro-organisms introduced at operation.

The various clinical and pathological observations on the liver were summed up in 1882 by Mangelsdorff, of Leipzig, who collected all the cases of cirrhosis of the liver which he could find recorded up to the date of publication of his own article. These cases he presented in abstract in the *Deutsches Archiv für klinische Medicin.* He reports altogether 321 cases of cirrhosis, and of this total number 184 cases were shown to be due to obstruction of the biliary passages, eliminating, moreover, all of these cases in which a certain or doubtful history of either syphilis or alcoholic intemperance might be supposed to have any decided action on the liver itself. Mangelsdorff concludes that there is no particular variety of cirrhosis which can be said to be dependent upon this disease of the bile passages, but that practically any condition of fibrosis of the liver can follow obstruction of the ducts.

In the literature since Mangelsdorff's compilation of cases—that is, from 1882 to 1900—we have been able to find only twenty-one distinct cases of cirrhosis of the liver due to obstruction of the biliary passages, if we exclude, on the one hand, those cases in which only a partial obstruction was associated with cirrhosis of this organ, and, on the other hand, those cases in which the statements of the writers are somewhat indefinite as to the exact pathological conditions. Thanks to the kindness of Dr. Merrill and Dr. Fletcher, of the Surgeon-General's Library at Washington, who allowed us to use their complete card catalogue, we have been able to bring this historical review up to May 1, 1900, and thus to present a fairly complete list of cases for the past eighteen years. To the twenty-one cases found already reported we may add three cases taken from the records of the Royal Victoria Hospital in Montreal, which show this condition in both the early and the late stages. The following is a list of the cases on record:

CASE I. (Maffucci. *Giornale Internationale della Scienze Mediche,* 1882, nouva serie, anno 4–2, Napoli, pp. 889–910).—Man; intense jaundice and ascites; liver soft on surface, olive-green, rougous, atrophied; cystic ducts dilated and containing a little liquid like egg albumen; common duct enormously dilated; hepatic duct slightly dilated. Below the common duct a band of connective tissue, which for 0.5 cm. compresses the duct. All lobules of the liver show connective tissue diffused about the parenchyma, which is diminished in volume; connective tissue between acini. Interlobular and intralobular cirrhosis.

CASE II. (same author).—Man; cancer of the pancreas pressing on the common duct; intense jaundice, ascites; liver small, surface soft, green; cystic and common ducts dilated. Head of pancreas transformed to a carcinomatous tissue, which completely occludes the common duct; all bile capillaries dilated. Interlobular and intralobular cirrhosis.

CASE III. (same author).—Woman; intense jaundice, ascites; carcinoma of stomach, with many secondary nodules in the peritoneum, one compressing the common duct at the point of union of cystic and hepatic ducts; hepatic and common ducts dilated; liver olive-green, atrophied, surface smooth, soft; all bile-ducts dilated and containing bile. Interlobular and intralobular cirrhosis of the liver.

CASE IV. (Heneage Gibbs. *Transactions of the Pathological Society of London,* 1883, vol. xxxiv., p. 129).—Male infant; family history good; born December 3, 1881; average development; jaundiced skin and conjunctiva a few days after birth; persistent clay-colored stools, emaciation, ascites; death July 10, 1882. At post-mortem, liver hard, smooth, weight 4 ounces; no common duct; occlusion of pancreatic duct; hepatic duct filled with fibrous mass; interlobular connective tissue much increased. Both interlobular and intralobular cirrhosis of the liver.

CASE V. (Henry Ashby. *Archives of Pediatrics*, 1884, vol. i., p. 537).—J. H., admitted to the Dispensary for Sick Children at Manchester, October 4, 1883. Family history negative; maternal, syphilis. Jaundice since birth; urine bile stained; stools clay-colored; liver enlarged, edge at umbilicus. Death December 30, 1883, aged four and a half months. At post-mortem all organs bile stained; no ascites; liver seven ounces, not enlarged, dirty-green color, surface granular, tough feel, creaking when cut. On section, dark-green islets of fibrous tissue, especially about the portal vessels. Small cystic duct entering the common duct and pervious to duodenum; no hepatic duct; bile-duct ending in fibrous tissue at the transverse fissure; microscopically fibrous tissue about the portal vessels. Both interlobular and intralobular cirrhosis.

CASE VI. (Alivia. *Contributo alla Casuistica della Cirrhosi Biliare*, Sassari, 1885).—Patient admitted November 13, 1883. Tumor in right hypochondrium, painful, fluctuating in size; pain in right hypochondrium, passing to epigastrium; nausea, vomiting, diarrhœa, jaundice; dark-colored urine; no clay-colored stools; irregular fever; death. At autopsy, perihepatitis, hepatic cirrhosis, biliary calculi, dilatation of bile channels, two gallstones in the gall-bladder.

CASE VII. (Michael. *Archives of Pediatrics*, 1885, S. 573; also *Archiv für Kinderheilkunde*, vii., 2, S. 137. Quoted by Gese).—Boy; jaundice since birth; clay-colored stools; dark-colored urine; great emaciation; death, second month. Liver not enlarged, green, creaks on cutting, strands of fibrous tissue through it; larger bile channels filled with bile; common duct ends in fibrous tissue.

CASE VIII. (Gessner. *Ueber Cong. Verschluss der Gallenausfuhrungsgange*, Halle, 1886. Quoted by Gese).—Boy; jaundice since birth; urine contains bile; feces colored; vomiting, cough, emaciation. Death, third month. Liver enlarged, grayish-green, hard, surface granular; connective tissue increased; cystic, hepatic, and common ducts obliterated except for pinpoint lumen in the common duct.

CASE IX. (Legry. *Bulletin de la Société Anatomique de Paris*, 1889, Anne 64).—E. C., female, May 9, 1889; aged fifty-seven years. At twenty years, in the sixth confinement, jaundice, pain in right hypochondrium and epigastrium; no clay-colored stools; chronic jaundice, œdema, and ascites; collateral circulation developed; urine quite dark. Post-mortem May 22d. Liver enlarged, surface granular, very hard, cuts with difficulty; bile channels dilated, contain biliary concretions; glands generally enlarged. An interlobular and an intralobular cirrhosis.

CASE X. (Cnopf. *Münchener medicinische Wochenschrift*, 1891, Nos. 16 and 17. Quoted by Gese).—Child; jaundice second day; white stools; urine containing bile-pigment. Death, tenth week. Liver normal in size, smooth surface; jaundiced interacinous and intra-acinous tissue increased; gall-bladder and duct quite lacking.

CASE XI. (Cnopf. *Münchener medicinische Wochenschrift*, 1891, Nos.

16 and 17. Quoted by Gese).—Child; three days jaundiced; urine icteric; grayish yellow, thin stools; emaciation; ecchymoses on face and neck; liver enlarged, sensitive; bloody diarrhœa. Death, thirty-third week. Liver enlarged, cirrhotic.

CASE XII. (Rolleston and Kanthack.[1] *Archiv für klinische Medicin*, 1892, p. 488).—Child, one month old; jaundiced; cystic disease of liver and kidney, with hypertrophic ciliary cirrhosis; bile passages much dilated, connective tissue about them much increased; great increase of bile-ducts; vacuolization of liver cells. Cirrhosis of liver; no definite obstruction of ducts.

CASE XIII. (Parkes Weber. *British Medical Journal*, April 25, 1895, p. 1027).—Mrs. M. S., aged fifty-five years; jaundice four years; pain in left side; no hepatic colic, no children, no miscarriages, no syphilis, no alcohol (?); xanthelasma palpebrarum. Liver hard, uniformly enlarged; œdema of feet and ankles; dulness of liver from fifth rib to level of umbilicus; pruritus; later, ascites; liver not to be felt; stools colorless or mixed with blood; urine contains bile; no dilatation of abdominal veins; temperature 100° F. Coma and death, December 24, 1895. At post-mortem, liver 54 ounces, tough, surface puckered or granular, green; gall-bladder dilated, hypertrophied, contains green fluid; cystic and hepatic ducts pervious, common duct dilated; two black gallstones in ampulla of Vater, size of cherry-stones; no ulceration; contents of gall-bladder could be squeezed into the duodenum. *Microscopical Examination.* Multilobular cirrhosis; no multiplication of smaller bile-ducts (liver presents ordinary cirrhosis, type of hypertrophic cirrhosis due to gallstones). Author compares Charcot's case, *Archives de Physiologie*, second series, vol. iii., p. 295.

CASE XIV. (Chadwick. *British Medical Journal*, 1895, vol. i., p. 1143).—Woman, aged thirty-six years; copious hæmatemesis; jaundice and gallstones six years; atrophy of liver; xanthelasma; liver green, much cirrhosed, fibrous tissue like ordinry cirrhosis.

CASE XV. (Gese. *Jahrbuch fur Kinderheilkunde und physiche Erziehung*, N. F., 1896).—Twenty-five cases of occlusion of the bile-ducts, with a number of cases of cirrhosis of the liver.

One new case reported: Child; jaundiced eighth and ninth day; clay-colored stools; urine containing bile-pigment; liver enlarged. At autopsy, obliteration of hepatic duct; patent common duct; open gall-bladder, fluid from gall-bladder passing into duodenum; liver cirrhotic; cirrhosis irregular, both interlobular and intralobular in type.

CASE XVI. (Stevens. *Archives of Pediatrics*, 1896, vol. xiii., p. 733). —Wm. McA., aged four months; family history negative; jaundice at birth; stools clay-colored; urine clear, green; later, blood in vomitus and stools, which became black and tarry. Death from hemorrhage. At autopsy, absence or obliteration of hepatic and cystic ducts; cirrhosis of liver; hemorrhage into stomach and intestines; deep jaundice; cystic, hepatic, and common ducts transformed to fibrous cords, absolutely impervious. Liver large, dark green on section, marbled, free surface granular.

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[1] In the above case of Rolleston and Kanthack no definite obstruction of the bile passages could be detected. Nevertheless, the dilatation of the biliary channels was so marked and the type of cirrhosis was so similar to that seen in the cases in which a positive obstruction could be demonstrated, as was shown by the illustration in their paper, as to make it quite proper to include their case in this list of cases of true obstructive cirrhosis.

Histological Examination. Cirrhosis of liver, involving groups of lobules (multilobular, possibly interlobular). Bile-ducts much increased.

CASE XVII. (Kynoch. *Edinburgh Medical Journal,* 1896, vol. xvii., pp. 35–37).—Matilda C., aged three months and four days, admitted to Dundee Royal Infirmary at two and a half months; jaundice since birth; skin and conjunctiva green color; emaciation; abdomen distended; liver enlarged, edge sharp; no ascites. At post-mortem, liver 237 grammes (8 ounces), edges sharp, green, tough in consistence, surface irregular, fibrous bands of yellow color; common duct, at junction of cystic and hepatic ducts, narrow, thread-like, just pervious to bile. Microscopically, slight biliary cirrhosis.

CASE XVIII. (Krokiewiez. *Wiener klinische Wochenschrift,* 1898, pp. 321–323).—M. S., aged fifty-seven years; jaundice; anorexia; constipation; pain in abdomen one year; chills at onset; œdema of legs, emaciation, and ascites; liver enlarged, painful, border 12 cm. below right costal margin, edge hard and thick, surface smooth; urine bile stained; tumor in region of gall-bladder; jaundice one year; ascites. Coma and death, August 14, 1897. At post-mortem, dilatation of common, hepatic, and cystic ducts; stenosis of common duct. Liver 3 cm. below costal margin, surface smooth, edge broad, capsule thickened, parenchyma hard, greenish-brown; bile-ducts dilated; gall-bladder enlarged, wall thick, contains few gallstones. Interlobular cirrhosis of liver; stenosis of common duct.

CASE XIX. (Boinet. *Archives Génèrale de Mèdecine,* 1898, vol. i., p. 385).—W., aged thirty-five years; alcoholic, non-syphilitic; gastro-intestinal catarrh and dysentery. First seen in 1894; jaundice six years; xanthelasma palpebrarum on both sides; urine high-colored; stools not clay-colored; for two and a half years liver constantly increased in size, reaching from the fifth intercostal space to within 4 cm. of crest of ilium; no ascites; no dilatation of abdominal veins. In 1896, extreme emaciation. Death from tuberculosis. At post-mortem, liver large, smooth, 4720 grammes (not hobnailed); lymphatic glands all enlarged, especially about hilus of liver, where they press on the common duct; liver cirrhotic.

CASE XX. (Rabé. *Cirrhose Periportal avec Calcul Enclave dans l'Ampoule de Vater. Mort par Pylephlebite Obliterante,* February, 1898).—Man, aged seventy-three years. Symptoms of atrophic cirrhosis and ascites. Liver 7 cm. in mammary line; contracted; dilated abdominal veins, jaundice of skin and conjunctiva; urine deep yellow; emaciation, œdema of legs and scrotum, constipation, anorexia; stools normal. Death from marasmus after five months. At post-mortem, 1200 c.c. of abdominal fluid; liver, type of Laennec's cirrhosis, very hard, chamois-gray, surface granular; hepatic, cystic, and common ducts dilated; calculus in common duct, another in ampulla of Vater. Periportal and interlobular cirrhosis, with great increase of bile-ducts.

CASE XXI. (Benner. *Ein Fall von Gallenstauung-cirrhose der Leber nach primaren Adenocarcinom im Ductus Choledochus.* Inaugural Dissertation, 1899).—Post-mortem, typical cirrhosis of the liver. Dilatation of bile-ducts: adenocarcinoma of common duct; retention of bile in duct. Interlobular cirrhosis about ducts; jaundice of all organs; great dilatation of all small bile-ducts. Liver enlarged and cirrhotic, weighing 2210 grammes.

Case XXII. (hitherto unreported).—Private case occurring in the practice of Dr. D. J. Evans, of Montreal. Male child, born of healthy parents, November 29, 1897. Breast-fed; digestion always bad; stools greenish; eczema capitis at three months of age. One month later, tuberculous glands of neck, caseous and suppurating. At a year and a half child became fretful and irritable; urine high colored; stools green; abdomen somewhat increased in size. One month later jaundice of conjunctivæ, clay-colored stools, great enlargement of abdomen, hypertrophy of liver, edge at crest of ilium; enlargement of spleen; later, contraction of liver, surface rough and lobulated. Development of œdema of extremities; congestion of abdominal veins, ascites, wasting, and emaciation; skin lemon-yellow in color; many petechiæ over palms, neck, and chest. Abdomen tapped and 24 ounces of clear, yellowish fluid removed. Collection of ascitic fluid almost immediately; emaciation and wasting extreme; great cachexia. Death, July 14, 1899.

The autopsy was performed by Dr. Anderson, of Montreal, examination of abdominal organs only permitted. Deep jaundice of skin and conjunctivæ, numerous petechiæ of skin of abdomen; large amount of ascitic fluid; pale yellow in color. Great hypertrophy of spleen; enlarged inflammatory gland at hilus of the liver pressing on the common duct, completely obliterating its orifice; liver greatly enlarged, surface made up of large lobules of liver substance lying between dense, firm bands of connective tissue, surface very rough. On section, liver cuts with difficulty, showing a great increase of fibrous tissue, which lies in islands between the hepatic lobules. Interlobular and intralobular cirrhosis of the liver.

Microscopical Examination of Liver. The capsule is thickened, with some infiltration of small round cells. Just underneath the capsule is a layer of fibroblasts, the protoplasm of which stains lightly with eosin, and the spindle-shaped nuclei stain deeply with hæmatoxylin. From the capsule the connective tissue has extended throughout the whole organ, lying in broad bands between the hepatic lobules, which are thus marked off into smaller or larger areas of normal liver substance. The strands of new tissue are made up of well-developed fibres and young fibroblasts. At the periphery of the organ bands of tissue join the capsule almost at right angles, and there spreading out into broad bundles round off or top off the hepatic lobules.

In the portal spaces the fibrous tissue has developed concentrically about the bloodvessels and bile-ducts, which are considerably dilated. Close to the vessels the tissue forms a ring of well-developed, rather lightly staining, fibrous tissue, in the periphery of which, where the process is less advanced, may be seen a layer of fibroblasts. These fibroblasts are especially abundant, extending everywhere, from the older deposit of fibrous tissue into the liver lobules, isolating and surrounding groups of liver cells. At times these fibres spread out between the hepatic elements, giving an appearance much like the branching of a tree. Throughout all the lobules, moreover, between the individual liver cells, may be seen isolated fibres of connective tissue—the cirrhosis is thus both *interlobular* and *intralobular* in type.

Coincidently with the deposit of fibrous tissue definite changes have occurred in the liver cells; near the centres of the lobules the cells are normal in size, the protoplasm is well preserved, and the nuclei are lightly stained with hæmatoxylin. At the periphery the cells are atrophied and compressed by the fibrous tissue, the protoplasm has almost entirely disappeared, and the nuclei are greatly shrunken. The liver cells thus are in a state of chronic inflammation, or, more properly, have degenerated to their earlier epithelial type. Where the layer of fibroblasts is especially abundant the liver cells are still more atrophied, there remaining practically only the nuclei, which are lined up in tubules or cords and surrounded by the new tissue. These nuclei are somewhat compressed and stained a little more deeply than the normal nucleus of the liver cell. These *cords* or *tubules* of cells, formed of little more than nuclei, are the elements which have been called *bile-ducts, bile capillaries,* or more recently *intermediate* or *pseudo-bile-ducts.*

The source of origin of these reduplicated bile-ducts has been in doubt for some years. It is maintained, on the one hand, that these ducts originate from the reduplicated epithelium of the older bile-ducts, while, on the other hand, their origin from compressed atrophied liver cells has been especially emphasized within the past decade. Findlay, who uses the term *intermediate* or *pseudoducts,* considers that they are simply liver cells which have degenerated and assumed the character of primitive hepatic elements, and later come to be connected with the normal bile-ducts. In the present case the origin of these reduplicated bile-ducts from liver cells is readily seen. It is possible to trace all the stages from the normal liver cells to the chronically inflamed liver cells with deficient protoplasm, and then to the rows of liver nuclei lined up in cords or tubules between the layers of fibrous tissue, and presenting an appearance quite similar to that of normal bile-ducts.

This reduplication of bile-ducts has reached an extreme grade in this case; they are especially abundant at the edge of the lobule in the zone of fibroblasts, where the new tissue seems to be surrounded by a wreath of ducts, outside of which lies the normal hepatic parenchyma. This wreath-like arrangement is observable in all the portal spaces; it seems more marked in this disease than in any other pathological conditions of the liver, and may possibly form a histological feature characteristic of obstructive cirrhosis and differentiating it from other varieties of cirrhosis of this organ. (See Fig. 1.)

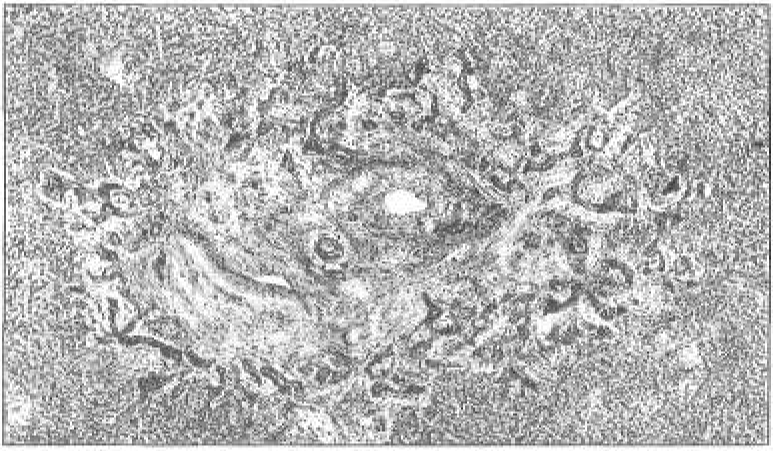
The strands of new tissue are infiltrated with small round cells, this infiltration being especially rich in the layer of fibroblasts, where the wreath of bile-ducts is to be made out. There are many small round cells as well scattered irregularly through all the new fibrous tissue and deposited between the liver cells in the centres of the lobules; in some areas the strands of new tissue are so infiltrated with small round cells as to suggest an inflammatory origin for the fibrous tissue present.

The walls of the larger bloodvessels are thickened and their lumen filled with blood cells. The smaller bloodvessels are occasionally dilated and in a state of acute inflammation, about the vessel wall being seen a deposit of round cells, with a few connective tissue nuclei. The central veins of the lobules are everywhere dilated; the lobules themselves are congested, often the red blood-corpuscles being massed together in large numbers between the hepatic elements.

The bile channels are dilated and full of brownish-black bile pigment, which is deposited irregularly throughout the bile passages of the whole organ. As a rule, this deposit of bile is most marked about the centres of the lobules, where often the liver cells are themselves stained yellow with the liver secretion. A similar precipitate of bile-pigment may be observed in the portal spaces and at the edges of the lobules.

Aside from the precipitate of bile-pigment, in many areas of this liver may be seen fine, *black granules, coccoid or diplococcoid in shape, which* are deposited both intracellularly and extracellularly. The interpretation of the nature of these bodies is exceedingly difficult unless one considers that they are micro-organisms in the progress of disintegration. This view is strengthened by the appearance of the bile-ducts in this case, which are in a state of active inflammation, their lumen being filled with well-formed bacilli. An etiological relationship between these granules and the new tissue developed in this liver was suggested by this appearance, but such a relationship was not confirmed by the examination of later cases of obstructive cirrhosis.

FIG. 1.



Specimen hardened in Müller's fluid, embedded and sectioned in paraffin stained with hæmatoxylin and eosin. Magnification 105 diameters. Between the hepatic lobules surrounding the portal vessels is seen the new-formed fibrous tissue in concentric rings, at the periphery of which lies the wreath of reduplicated bile-ducts. Slight infiltration with leucocytes. Brownish deposit of bile pigment in the liver parenchyma. Interlobular and intralobular cirrhosis.

CASE XXIII. (hitherto unreported).—Maud V., aged twenty-eight years, admitted to the Royal Victoria Hospital, November 25, 1898; died December 22, 1898.

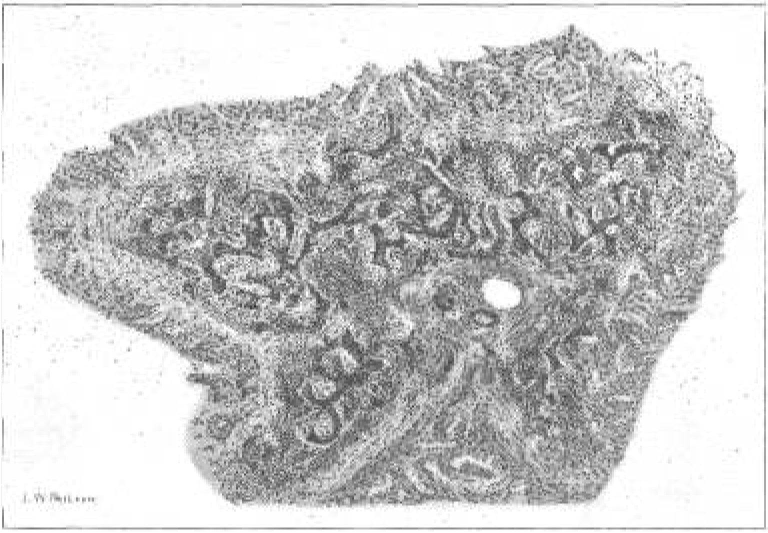
History. Jaundice three years, increasing in intensity; pruritus of skin; clay-colored stools; tenderness in right hypochondrium; anorexia; vomiting, vomitus greenish in color; œdema of the legs; dilated abdominal superficial veins; ascites; hydrothorax; coma and death.

At post-mortem, liver greatly enlarged, weighing over 4000 grammes, surface granular; liver firm, on section cutting like leather; gall-bladder thickened; cystic duct obliterated; hepatic duct slightly dilated, containing a loose calculus pressing on the cystic duct at its orifice. Interlobular and intralobular cirrhosis of the liver.

Microscopical Examination. The morbid changes seen in this liver are quite similar to those seen in the preceding case, but somewhat less advanced in their development. Between the hepatic lobules there are broad bands of tissue, made up of well-developed connective tissue fibres, in the periphery of which are many fibroblasts which penetrate the lobules between the liver cells, isolating and surrounding individual groups of cells. The cirrhosis is both interlobular and intralobular in character.

In the portal spaces where the tissue has developed in concentric rings about the bloodvessels and the bile channels one sees a zone of lightly staining, well-formed fibrous tissue, surrounded by a layer of fibroblasts, in the periphery of which lies a wreath of reduplicated bile-ducts. Outside this wreath lies the normal hepatic parenchyma. This wreath-like arrangement is visible in this liver in many of the portal spaces, but more frequently between the hepatic lobules the bile-ducts are lined up at right angles to the strands of fibrous tissue. (See Fig. 2.)

FIG. 2.



Specimen hardened in Müller's fluid, embedded and sectioned in paraffin stained with hæmatoxylin and eosin. Magnification 70 diameters. Moderate development of fibrous tissue between and within the lobules. Considerable infiltration with leucocytes. Wreath-like arrangement of reduplicated bile-ducts. Interlobular and intralobular cirrhosis.

In the centres of the lobules the liver cells are still preserved, but at the edges of the lobules they are atrophied and compressed. One sees the same transition from the normal liver cells to the chronically inflamed liver cells and thence to the reduplicated bile-ducts; there is no vacuolization and no fatty degeneration of the liver cells.

The walls of the larger bloodvessels are slightly thickened, the smaller bloodvessels being somewhat dilated; the central veins are especially enlarged and the liver lobules are markedly congested throughout, many red blood-corpuscles lying free among the hepatic elements. The escape of blood in some cases has been so marked as to suggest capillary hemorrhages.

The bile channels are not dilated; there is no special deposit of bile pigment, and only a few liver cells are seen which are slightly stained with bile.

The infiltration with leucocytes is very marked, especially in some of the strands of new tissue, where the deposit of both polymorphonuclear and small mononuclear leucocytes is so extensive as to again suggest an inflammatory origin for the tissue changes. This infiltration, moreover, is especially abundant about the new bile-ducts, but in the lobules themselves, between the liver cells, are often found many isolated small round cells.

The characteristic appearances of biliary cirrhosis are thus seen in this case as well as in the preceding one, and while the presence of leucocytes is strongly suggestive of inflammation, yet there are no bacteria present in any of the bile-ducts and no especial deposit of coccoid or diplococcoid bodies in or between the liver cells.

CASE XXIV. (hitherto unreported).—Walter B., aged fifty-three years, admitted to the Royal Victoria Hospital, November 14, 1899; died November 19, 1899.

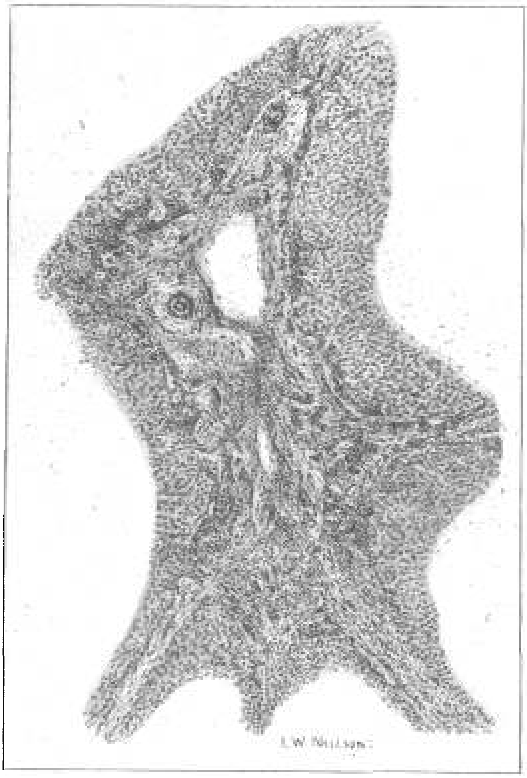
History. Attacks of pain in the epigastrium, tenderness, and vomiting, over a period of two years; jaundice; clay-colored stools; bile-stained urine; enlargement of liver and tenderness over gall-bladder; marked itching of skin. Operation: cholecysduodenostomy. Death from hemorrhage.

At post-mortem, liver yellow, granular, firm, and enlarged, on section cutting with difficulty, showing islands of fibrous tissue; cystic, hepatic, and common ducts greatly dilated; ulceration about the ampulla of Vater, especially on the duodenal side, where there is a slight tear in the mucous membrane and an ulcer about the bile papilla, showing recent passage of gallstone; no calculus found at operation or at autopsy. Interlobular cirrhosis of the liver.

Microscopical Examination. (See Fig. 3.) The histological changes seen in this liver are indicative of an early stage of cirrhosis, dependent upon obstruction of the bile passages. The development of fibrous tissue is little marked, but between the lobules may be seen a number of strands of thickened connective tissue. This tissue has not encroached to any extent on the liver cells, and there seems to be comparatively little development of fibrous tissue in the lobules themselves. The tissue itself is largely made up of fibroblasts, with spindle-shaped nuclei. This tissue is specially well developed about the portal spaces, where it is very rich in nuclei. In a few of the portal spaces a concentric arrangement of this tissue about the portal vessels and the dilated bile-ducts may be observed, and a similar zone of fibroblasts, with a wreath of reduplicated "bile-ducts," is seen about the older fibrous tissue. The number of these bile-ducts is quite small, however, and the wreath-like arrangement is only observable in a few areas. The infiltration with leucocytes is especially great in the strands of new tissue; in many of the liver lobules there is a rich deposit of leucocytes among the liver cells, especially at the edge of the lobules.

The bloodvessels are everywhere dilated, both in the portal spaces and in the centres of the lobules. The walls of these vessels are considerably thickened and their lumen filled with red blood-cells. About the central veins there is a rich deposit of fibrous tissue infiltrated with mononuclear leucocytes; here the liver cells are greatly atrophied and have in many cases quite disappeared. In the periphery of the lobule as well the liver cells are shrunken and chronically inflamed.

FIG. 3.



Specimen hardened in Müller's fluid, embedded and sectioned in paraffin stained with hæmatoxylin and eosin. Magnification 70 diameters. Deposit of fibrous tissue between the liver lobules. Marked infiltration, with leucocytes. Moderate reduplication of bile-ducts, which show the wreath-like distribution. Interlobular cirrhosis.

The bile-ducts are everywhere dilated and full of bile. A deposit of bile-pigment has taken place in many of the liver cells about the central veins of the lobule, where often these cells are stained yellow with this pigment. A radial distribution may often be made out about the dilated central veins.

The microscopical changes in this case reveal a cirrhosis of the liver, interlobular in character, the fibrous tissue having developed about dilated bile channels. The dilatation of these channels and the deposit of bile-pigment is so great as to indicate a long-continued obstruction to the flow of bile, such an obstruction evidently being the etiological factor concerned in causing the cirrhosis.

Analysis of the Above Cases.

CAUSES OF OBSTRUCTION. *Congenital Deficiency of Bile-ducts.* The most frequent cause of complete obstruction to the flow of bile is the congenital deficiency of the hepatic and cystic ducts, these ducts terminating in blind, impervious cords. The livers of these congenital cases are enormously enlarged, the edge often reaching to the anterior-superior iliac spine, the enlargement either being observed at birth or taking place within a few weeks after the entrance into life. The children subject to this disease develop deep jaundice, profound cachexia, emaciation, ascites, œdema of the extremities, and various cutaneous disorders. They usually die at the age of six or eight weeks.

At autopsy the livers are found to be greatly enlarged, with a rough, hard surface. On section they cut with difficulty, show dilated bile channels full of bile and islands of connective tissue. Microscopical examination reveals an interlobular cirrhosis of the liver of an extreme grade, with great reduplication of the smaller bile-ducts. Death intervenes in these cases within a few weeks after birth, and in spite of the extreme and persistent jaundice which one observes a suspicion arises that the retention of bile is not the cause of the cirrhosis of the liver, but that the increase of the fibrous tissue in this organ is the result of the same intra-uterine morbid change which leads to the obliteration of the ducts. It must be remembered, however, that the liver is probably an active functional gland after the third month of pregnancy, and we thus have a lapse of time sufficient for the cirrhosis to develop in consequence of the obliteration of the ducts alone and the subsequent damming back of bile and its action on the liver cells without calling to our aid in explaining this condition any unknown etiological factors.

Gallstones. Gallstones stand next in order of frequency to the cases of congenital deficiency of the ducts. Here a complete obstruction to the flow of bile may be caused by the filling of the gall-bladder by a number of stones, by the lodgement of a single stone in one of the ducts or in the ampulla of Vater, or, more frequently still, by the contraction of scar-tissue which has developed about an ulceration caused by the passage of a sharp-edged gallstone. In some one of these ways the flow of the liver secretion is entirely shut off, and at autopsy the livers of these patients show a cirrhosis interlobular in character and usually moderate in extent. If the obstruction be of long standing a more advanced state of cirrhosis may be developed, the fibrous tissue developing both between and in the hepatic lobules.

It has been stated by some writers that in gallstones cirrhosis of the liver seems to develop more frequently in connection with rough, sharp-edged stones than in connection with round, smooth stones, which are less capable of causing inflammation and ulceration of the biliary passages.

Cancer of the Head of the Pancreas occurs rarely as a cause of obstructive biliary cirrhosis. Several cases have been reported, however, of this variety, either by Mangelsdorff or in the list of cases quoted in this article. The growth of cancerous tissue in the pancreas completely obliterates the lumen of the common duct, and thus causes a complete obstruction to the flow of bile, inaugurating the same series of morbid changes in the liver as is seen in the other cases.

Enlarged Glands at the hilus of the liver exerting a pressure on the common or the hepatic duct in rare instances may block the liver secretion sufficiently to cause cirrhosis of this organ. This is the condition seen in one of the cases studied at the Royal Victoria Hospital. The glands may be cancerous, tuberculous, or simply inflammatory in nature, and the livers of these cases may show both the presence of metastatic tumor nodules and an increase of the fibrous tissue about the dilated bile channels between the lobules of hepatic cells.

MACROSCOPICAL APPEARANCE. The livers in these cases of obstructive cirrhosis are greatly enlarged, with a rough, jaundiced surface, and considerable perihepatitis. The weight of the liver is much increased, the organ hard, cutting with great difficulty, and showing on section greatly dilated biliary passages and islands of new connective tissue.

In the later stages the contraction to which all cirrhotic livers are probably liable takes place in this variety of cirrhosis in a large proportion of cases, and, in fact, these livers often approach more nearly the type of cirrhosis seen in the atrophic liver of Laennec than they do the enlarged hypertrophic organ of Hanot. The development of ascites, œdema of the extremities, and the caput medusæ of abdominal veins in many cases indicates the great obstruction to the flow of blood in the portal bloodvessels caused by the large amount of fibrous tissue present in the liver.

MICROSCOPICAL EXAMINATION. Careful histological study reveals dilated bile channels, dilated bloodvessels, an increase of fibrous tissue about these dilated channels, and a cirrhosis of the liver which may be either interlobular, intralobular, or pericellular in type. As has already been indicated, groups of cells or individual cells are often seen isolated and surrounded by fibrous tissue. The presence of new bile-ducts is noted in nearly every careful anatomical description, although the wreath-like distribution of bile-ducts has not been emphasized in any cases except those studied in Montreal. It is impossible as yet to say whether this wreath-like distribution is peculiar to this variety of hepatic cirrhosis, but its occurrence in all three of the cases here reported leads to the suggestion that it may be characteristic of this disease, differentiating it histologically from other morbid conditions of the liver.

I use the term bile-ducts here to indicate those smaller bile channels lined by cubical epithelium as distinct from bile capillaries lying between the liver cells and lined by flat epithelium. The presence of these reduplicated bile-ducts cannot be considered diagnostic of any variety of cirrhosis of the liver, as they have been described in practically all varieties of this disease, in hydatids of the liver, and in certain intoxications. Wagner and Liebermeister have noted them in cases of gallstones, in alcoholic cirrhosis, and in chronic obstruction of the hepatic veins; they have been described in liver abscesses, in the syphilitic liver of Friedländer, and in chronic tuberculous peritonitis. Podwyssozki has observed them in regenerating liver tissue, and it has recently been shown by Neisser, of Leipzig, that the experimental injection of phenol solution and substances like phosphorus into the circulation is followed by the appearance in the liver of these new-formed bile-ducts.

Ackermann has shown by injection that these columns or tubules of cells described under the name of ducts are in reality bile channels, for he has been able to trace a direct connection between them and the larger bile passages.

Recently, Findlay has called renewed attention to the mode of formation of these new bile-ducts, regarding them as simply liver cells, degenerating and reverting to their embryonal or epithelial type and later coming to be connected with the older bile passages. He proposes to name them *intermediate* or *pseudo-bile-ducts.* Although their origin from chronically inflamed liver cells has been specially emphasized within recent years, and although this mode of origin is quite clearly indicated in the cases studied in this report, it must be remembered that there are many pathologists who still maintain that these new ducts are formed by the simple reduplication of the epithelium of the older bile-ducts.

CLINICAL SYMPTOMS. In studying the histories of these cases of obstructive cirrhosis one is impressed by the great similarity which the symptoms of the different patients bear to each other, such a similarity being so marked as to reveal a symptom-complex and a cycle of clinical changes which are quite characteristic of a complete obstruction to the flow of bile and the morbid changes subsequent to this obstruction. The history of any one case, in fact, is repeated in the histories of practically all of the other cases.

The onset of the disease is sudden, the first symptom being an extreme jaundice, coincident with which is the appearance of clay-colored stools, which indicate the complete stoppage to the flow of bile and the retention in the blood and lymph of the patient of this liver secretion. Enlargement of the liver follows immediately, often reaching an extreme grade, the edge being found at the anterior iliac spine. The systemic disturbance now becomes marked, due doubtless to the incompetence of the liver and absorption of the liver secretion. The headache is painful and severe, often intermittent in occurrence; the anorexia is complete, so that the patient may be able to take no food whatever, *the vomiting being frequent and exhausting, the ejecta a greenish* detritus or bile-stained gastric secretion. With the appearance of the gastro intestinal changes the various forms of cutaneous disorders develop, especially xanthelasma and subcutaneous hemorrhages. The itching of the skin is extreme, so great as to require large doses of morphine as a sedative. Fever is rare, and in fact does not occur in the cases of persistent obstruction to the flow of bile, it usually being seen in allied cases of an intermittent obstruction caused by the lodgement of a calculus in the ampulla of Vater, when usually paroxysms of chills, fever, and sweating develop, followed by partial relief of the jaundice. The emaciation and wasting are very rapid, the loss of strength and flesh taking place within a few weeks after the onset of the first symptoms.

The condition in which these various symptoms are included has been described as cholæmia, but a better definition is found in its description as *hepatic incompetence* and *auto-intoxication.* As a result of the complete stoppage to the flow of bile and the retention of this substance by the system, the liver is permanently put out of function, the retained products of digestion, instead of being further broken up and eliminated, are, together with the liver secretion, absorbed by the general circulation, and act through the blood and lymph on all the different organs and tissues of the body.

Following the enlargement of the liver we have a subsequent contraction of this organ, which occurs with great rapidity, and the appearance of which ushers in the chain of symptoms which quickly results in death. The size of the liver greatly diminishes, the fibrous tissue developing in it blocks the portal circulation and causes the dilatation of the abdominal veins (during the establishment of a compensatory circulation), œdema of the extremities, and abdominal ascites. The occurrence of the last three symptoms is common to practically all of these cases of obstructive cirrhosis, and, as we shall point out below, they are symptoms differentiating this variety of disease from the ordinary cirrhosis of the liver in which jaundice is present.

The patients subject to this disease suffer from the greatest weakness and emaciation, unable to retain food in consequence of the persistent vomiting, developing marked cutaneous disorders, and in the late stages œdema and ascites, quickly sink into a profound coma or a toxic condition, the end of which is seen only at the fatal exit.[1]

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[1] It is difficult to explain the statements of several writers who allude in their description to clay-colored stools and bile-stained vomitus: the presence of bile in the gastric secretion may be accounted for, if we assume a secretion of this substance by the walls of the stomach, as

General Considerations. In considering these cases of cirrhosis of the liver associated with complete obstruction of some one of the ducts of this organ and subsequent damming back of bile on the liver cells several problems naturally present themselves:

Can obstruction to the flow of bile cause in man and animals a cirrhosis of the liver, and by what means is such a cirrhosis caused?

Is the type of cirrhosis associated with obstructions in man to be differentiated on pathological and clinical grounds from other varieties of cirrhosis of this organ?

Let us now consider those questions in their various aspects.

As we have indicated above, many experiments have been performed which seem to show that cirrhosis of the liver is in *animals* a direct consequence of ligature of the common bile-duct or its branches. In the earlier experiments, however, although the increase of fibrous tissue was always found to follow this ligature of the ducts, yet the operators conducted their experiments without modern methods, and in many cases infected their animals at the time of operation. It is noticeable in nearly every series of cases reported that a large proportion of animals died from sepsis, and it thus was impossible to decide whether the cirrhosis seen was a consequence of the damming back of bile caused by the ligature of the ducts or followed the infection of the liver and the bile passages by micro-organisms introduced at operation.

Beside the work of Legg and Charcot, already referred to, a number of pathologists have worked in this field at different periods.

Maffucci, of Naples, reported a series of experiments in which he ligated the common duct in a number of animals which lived about one month and showed at autopsy a typical interlobular cirrhosis.

Julius Steinhaus, who operated on guinea-pigs, found after ten days dilated bile-ducts and necrotic areas in the liver cells, but found no increase of bile-ducts and no increase of connective tissue in the liver. A lapse of ten days between the operation and autopsy cannot be considered as sufficient time for any great amount of cirrhosis to develop in connection with obstruction, and the failure of Steinhaus to find it is not strong evidence of a negative character.

The recent work of Vaughan Harley is quite conclusive from the experimental stand-point in answering the question whether obstruction does or does not cause cirrhosis of the liver. With the most perfect antiseptic technique Harley ligated the common duct or its branches in a number of animals, which he allowed to live for a considerable time after operation, either killing them at a late date or waiting until death

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the blood and lymph channels are naturally highly charged with it. It must be remembered, however, that many of the observations of earlier writers as to the presence of bile in the vomitus were made simply from the visual appearances of the ejecta, and not from careful chemical tests.

should ensue from the morbid changes caused by the obstruction. In practically every case Harley found a definite increase of connective tissue in the liver about the bile-passages—that is, a true interlobular cirrhosis—moreover, there was no evidence that he had at any time infected the liver or any of the bile channels.

It is interesting in this connection that Nicoti and Richaud have described in dogs a condition of biliary cirrhosis of the liver dependent on the presence of gregarines in the branches of the hepatic duct. Complete obstruction of these branches is thus caused, with the resulting dilatation of the ducts behind this obstruction and a growth of connective tissue about these dilated passages. There are numerous new-formed bloodvessels and new-formed bile-ducts in the connective tissue.

Macroscopically the livers are enlarged and cirrhotic, cutting with great difficulty and showing considerable fibrosis. We have thus a condition of obstructive biliary cirrhosis in animals quite similar to that seen in man, and yet not caused by any experimental interference.

In *man* the question of the positive causation of cirrhosis of the liver by the obstruction to the flow of bile naturally has a different aspect, inasmuch as we are unable to produce experimentally this obstruction and to note the changes in the liver which would follow from it. We are, therefore, compelled in answering this question to examine the number of cases in which cirrhosis of the liver is seen in connection with a pathological obstruction to the ducts of the liver and to bring evidence in favor of the etiological relationship between the two by the number of cases of this combination which can be found.

Mangelsdorff, in 1882, reported 184 cases in which cirrhosis of the liver was associated with an obliteration of the bile-duct and in which there was no evidence that there were other etiological factors involved in causing this cirrhosis. Since 1882 we have been able to find twenty-four more cases in which as well an obliteration of the ducts of the liver seem to be the only causative agency in producing the chronic interstitial hepatitis. In all of these cases the usual factors of alcohol, syphilis, and poisonous intoxications which are seen in cirrhotic cases may be eliminated by careful study of the case-reports.

We thus have a total of 208 reported cases of cirrhosis of the liver in which the complete retention of the hepatic secretion and its subsequent action on the hepatic parenchyma is the only factor which can be shown to have any etiological influence in producing this cirrhosis.

This number at first sight seems rather small, especially that collection of cases since 1882; but if we remember, however, that Mangelsdorff's report includes all of the cases reported from 1822 to 1882, and that a very large amount of the work done on the liver occurred in the decade from 1870 to 1880, the apparent discrepancy between the number of cases reported up to 1882 and since then is thus explained. Moreover, cirrhosis of the liver itself is comparatively rare, and to be able to quote a series of over 200 cases in which the factor of obliteration of the ducts alone is the only agency which can be cited as causing the cirrhosis is sufficient, from a pathological stand-point, to show that obliteration of the ducts and cirrhosis of the liver are definitely associated as cause and effect.

ETIOLOGY OF THIS CIRRHOSIS SEEN IN OBSTRUCTION. There are various views as to the actual cause of the cirrhosis of the liver which has been noted in connection with obstruction to the flow of bile. Observers have been divided in their opinions, and have maintained, on the one hand, that the stasis of bile alone was sufficient to cause cirrhosis, and, on the other hand, that there was always an inflammation of the bile-ducts, subsequent to this stasis, which caused a new growth of connective tissue in the liver. Charcot maintained that the retention of bile alone by its action on the liver cells was quite sufficient to cause the fibrosis seen in this organ; but Litten, on the contrary, considered that obstruction alone would not cause cirrhosis, but that there was in all cases an inflammation of the walls of the ducts. The latter cited in favor of his view a number of cases of gallstones where the stones were round and smooth and had caused no inflammation of the ducts and no cirrhosis of the liver. He contrasted these cases with those in which the gallstones were rough and sharp-edged, and had caused an inflammation of the ducts and the subsequent development of fibrous tissue. Litten, as well, operated on a number of animals under antiseptic precautions, ligating the ducts, but obtaining no cirrhosis; he did obtain a cirrhosis, however, by the injection of croton oil and other irritating substances into the common duct.

As we have pointed out above, the association of cirrhosis of the liver and the presence of rough, sharp-edged gallstones is explained by the complete obliteration of the ducts caused by the ulceration of these stones and the subsequent growth of scar-tissue quite as well as by the inflammation of the bile channels.

Gerhardt, in 1892, who had noted after ligature of the ducts the presence of many necrotic areas in the liver cells, endeavored experimentally to explain these necrotic areas in cases where there was obstruction to the flow of bile. He took one set of animals in which he ligated the common ducts, estimated the pressure of bile behind the ligature, and found it to be between 2 and 4 cm. of water. The livers of these animals showed necrotic areas. He now repeated the experiment in another set of animals, but drew off the bile and passed salt solution into the ducts under a pressure of 50 cm. of water. The livers of these animals showed no necrosis, and he therefore concluded that it was the long-continued action of the bile on the liver cell which caused the slow cell death, not the pressure caused by the biliary stasis in the ducts themselves.

The *inflammatory origin* of the fibrous tissue seen in the livers of obstructive cirrhosis has been supported by a number of observations in which various micro-organisms were found in the liver. As we have stated above, in one of the cases in Montreal the number of these micro-organisms was so great as to lead to the belief that they might be a causal factor in producing the cirrhosis. Subsequent experiments, however, show that the majority of the livers of man and animals contain various forms of micro-organisms in their normal healthy condition, and, therefore, the mere finding of bacteria in cirrhotic livers cannot be considered as a proof that the cirrhosis is dependent upon the presence of these bacteria. In two at least of the cases studied here there was no evidence that bacteria were present to any greater degree than they are present in the normal hepatic parenchyma. Moreover, Vaughan Harley has recently sent to the Molson Pathological Laboratory in Montreal several specimens from the livers of the animals in which he had caused experimental cirrhosis. Dr. Adami has carefully studied these specimens in order to determine, if possible, whether micro-organisms are present or not, and he has uniformly failed to find any bacteria in these livers, either by the ordinary methods of staining, by Gram's method, or by the use of carbolthionin. It is natural to conclude, therefore, that from the experimental stand-point, at least, obstruction to the flow of bile will cause cirrhosis of the liver without infection of the bile channels.

In man, of course, this question has a somewhat different phase, for there is in practically all cases a considerable inflammation of the walls of the bile channels and often a slight inflammation of the smaller bloodvessels, the small-celled infiltration between the lobules often reaching an extreme grade, the appearance suggesting even the formation of small abscesses. Hence, it is impossible to find cases of cirrhosis of the liver in man associated with obstruction where one can say with certainty that the obstruction to the flow of bile has been the only factor concerned in causing the increase of fibrous tissue. We may thus conclude that the damming back of bile caused by the obliteration of the ducts does not always lead to the cirrhosis *per se*, but may lead to it as well by causing a certain amount of inflammation of the bile channels.

Even if we grant that the retention of bile and its poisonous action on the liver cells is the cause of the cirrhosis of the liver, we are still in some doubt as to the path which the bile traverses in order to come in contact with the hepatic parenchyma, for Vaughan Harley has recently shown that the jaundice which develops after the ligature of the bile-ducts will not supervene with the same rapidity if the thoracic duct be tied as well. Evidently the lymphatic circulation is the path by which the bile reaches the different tissues and organs of the body, and it may be possible that the bile may reach the liver cells by passing from the bile-ducts through the lymphatic circulation and back again into the liver cells themselves.

VARIETIES OF BILIARY CIRRHOSIS. Under the title of biliary cirrhosis there have been described at least three different conditions—the biliary cirrhosis of children in India, Hanot's cirrhosis or hypertrophic cirrhosis with jaundice, and the cirrhosis dependent upon obstruction of the bile passages.

The first variety has been emphasized especially by Gibbons and McNally, who have reported a number of cases from the poorer classes of the inhabitants of East India. The children subject to this disease show during life a painless enlargement of the liver, a voracious appetite alternating with anorexia, a languid, fretful disposition, great thirst, fever, splenic enlargement, constipation, and clay-colored stools, with jaundice and eventually ascites, increasing up to the time of death. At autopsy the livers are enlarged, bile stained, typically cirrhotic, their microscopical examination showing, moreover, a mixed interlobular and intralobular type of cirrhosis, with a great degeneration of the liver cells and many increased bile-ducts. The cirrhosis of this organ is very irregular, often single groups of liver cells, or even single cells, being isolated and surrounded or replaced by connective tissue. It is thus really a pericellular cirrhosis. The etiology of this variety is supposed to lie in the use of unsuitable food and in the subjection to bad hygienic conditions, to which the children of the poorer classes in India are especially liable. It is not impossible that, like Hanot's cirrhosis, to which this variety seems to bear some resemblance, the cause of the disease of the liver may be primarily infectious.

Hanot's Cirrhosis. The cases usually recorded under the title of *biliary cirrhosis* correspond with fair accuracy to the description given by Hanot of his *hypertrophic cirrhosis* with *jaundice*, and Hanot himself makes use of the terms biliary cirrhosis in describing the disease which he has named. In this disease the main clinical symptoms are dull pain in the region of the liver; acute attacks of abdominal pain, resembling hepatic colic; a slight jaundice, increasing after each attack; a gradual increase in the size of the liver and in the circumference of the abdomen, with the maintenance of fair general health and an excellent appetite for some time. The stools are not clay-colored, but the urine contains an abundance of bile pigment; there is no ascites and no enlargement of the abdominal veins, although there may be intestinal hemorrhage; the fever, at first slight, may become marked, the temperature rising in the evening to 102° or 104° F., and the pyrexia assuming the character of hepatic intermittent fever. The bodily strength is maintained, the emaciation is slow, and the course of the disease chronic.

There are, however, acute cases of Hanot's cirrhosis in which the patients die within a few months after their first observation by clinicians, having practically no jaundice and few biliary symptoms except an enlargement of the liver, but showing at autopsy a hypertrophic cirrhosis of the liver corresponding to the type described by Hanot, without obstruction to the flow of bile.

Pathologically, in Hanot's cirrhosis the liver is symmetrically enlarged and smooth; on section it cuts with difficulty, and has a jaundiced, dark-green appearance; the common and hepatic ducts are quite pervious and show no obstruction to the flow of bile, although the smaller ducts may be slightly dilated.

Microscopically, about the larger bile passages there is development of new fibrous tissue in concentric layers, this new tissue usually lying between the lobules, but at times penetrating within them, producing an intralobular as well as an interlobular type of cirrhosis. More frequently, however, the cirrhosis approaches the pericellular type—that is, there are individual groups of liver cells at the edges of the lobules, which are being cut off by the new connective tissue. There is a chronic diffuse angiocholitis and a periangiocholitis, but the new tissue is more of a replacement than of a productive inflammatory type.

We are in some doubt as to the etiology of Hanot's cirrhosis, and Hanot himself has not given any exact evidence to solve this problem. He has stated that the cirrhosis may be due to angiocholitis of the bile passages, to gallstones, and to obstruction to the flow of bile, and intimates that it may be infectious in origin. Goluboff, who has given the most accurate description of Hanot's cirrhosis published recently, attributes the fibrosis of the liver in his cases, which he described as biliary cirrhosis, to angiocholitis of the smaller bile-ducts, in which the retained bile causes a new growth of connective tissue between the lobules by the direct chemical or toxic action of the bile on the liver cells, the biliary stasis being due to the obstruction caused by the inflammation of the larger bile-ducts. The usual view, moreover, now maintained by the French school of pathologists is that Hanot's cirrhosis is caused primarily by infection, and is thus to be differentiated entirely from cases of cirrhosis of the liver seen in obstruction to the flow of bile caused by gallstones or by congenital obliteration of the bile-ducts.

COMPARISON OF DIFFERENT VARIETIES OF CIRRHOSIS. Let us now compare Hanot's cirrhosis with those cases of obstruction cirrhosis which we have described, to see, if possible, whether the two conditions can be differentiated on pathological and clinical grounds.

In Hanot's cirrhosis the liver is uniformly enlarged, the surface smooth, without perihepatitis, the contraction to which all cirrhotic livers are liable taking place in only a few isolated instances. It must be remembered, however, that there are cases in which patients pass through a cycle of symptoms characteristic of hypertrophic cirrhosis, with jaundice, and at autopsy reveal a small hobnailed liver; such cases are necessarily quite rare. The bile-ducts in this variety are seldom dilated, and when so only to a moderate extent, their lumen being always pervious.

In obstructive cirrhosis the liver may be enormously enlarged, as in the congenital cases, or it may approach in character the hobnailed liver of Laennec. There is usually considerable perihepatitis, the bile passages are always greatly dilated, and there is always, of course, a complete obstruction of some one of the ducts.

On section the livers in both diseases cut with great difficulty, revealing the presence of large amounts of new fibrous tissue distributed in islands between the hepatic lobules, the only difference between the two conditions here being the enormous dilatation of the bile-ducts which the obstructive cirrhosis reveals in contrast to the mild dilatation which Hanot's cirrhosis shows.

Microscopical examination reveals almost identical conditions in the livers of obstruction and the livers of ordinary hypertrophic cirrhosis with jaundice. In both cases the connective tissue develops about the bile passages, between the lobules of the liver, and may either lie between these lobules alone, causing an interlobular cirrhosis, or may penetrate within the lobules, causing an intralobular type. In both cases where the fibroblasts surround at the edge of the lobule individual liver cells the type of cirrhosis becomes more nearly that of a pericellular cirrhosis. There is the same inflammation of the smaller bile channels, the same congestion of the bloodvessels, and the same degeneration of the liver cells at the edge of the lobule. The reduplication of bile-ducts, as we have already shown, reaches an extreme grade in both cases. It is as yet impossible to say whether the wreath-like arrangement of these ducts which has been noted in cases of obstruction can be discovered as well in Hanot's cirrhosis, further study of the latter disease being necessary before any positive assertions can be made in regard to the appearance of this wreath-like distribution in hypertrophic cirrhosis with jaundice.

The autopsy findings in the two diseases differ only in the changes subsequent to the obstruction to the portal circulation which is seen in the cirrhosis of the liver dependent upon obstruction of the bile-passages—that is, œdema of the extremities, abdominal ascites, and a dilatation of the abdominal veins—a triad of symptoms which appears seldom or never in Hanot's cirrhosis.

From the *etiological* stand-point the two conditions naturally differ greatly in their causation: Hanot's cirrhosis is generally an infectious process—that is to say, the presence of the symptoms and the pathological findings of Hanot's cirrhosis are better explained by the supposed entrance of micro-organisms into the biliary passages than they are by any other known factors. The changes seen in obstructive cirrhosis follow invariably the complete obliteration of some one of the bile-ducts, but both in Hanot's cirrhosis and in the variety of cirrhosis which we are especially considering we are compelled to look to the inflammation of the smaller bile passages as being the immediate cause of the production of the fibrous tissue between the lobules of the liver.

We thus see that from pathological grounds alone the changes seen in the two varieties of cirrhosis are quite similar, and that it would be impossible from our present knowledge to say, on examination of any particular variety of cirrhosis of the liver, whether we were dealing with simple hypertrophic cirrhosis with jaundice or with a case of obstructive biliary cirrhosis.

Clinically, the symptoms of the two diseases differ in the widest extent in their occurrence, in their intensity, and in the rapidity with which the patients succumb to the morbid changes. In hypertrophic cirrhosis with jaundice we have a slow, chronic disease, where the general health is maintained for some time; emaciation and wasting are slow, the appetite good, with a little gastro-intestinal disturbance. The jaundice is insidious in its onset, the increase of the icterus being coincident with paroxysmal attacks of hepatic colic. The urine is loaded with bile pigment, although the bile always finds its way into the intestines, as is shown by the presence of bile-stained stools. The liver is enlarged throughout the whole course of the disease except in rare instances, and when the contraction of this organ occurs a small amount of ascites may develop. Fever is a constant, and, in fact, a characteristic symptom. It is intermittent in type and forms the basis for that pyrexia now constantly described as hepatic intermittent fever. The patient usually after a long period, during which he alternates between a fairly good state of health and attacks of colic, fever, and jaundice, very gradually loses his flesh and strength, and only at a late date succumbs to the disease process.

In obstructive cirrhosis, however, the clinical picture is absolutely different: the disease is acute in its onset and in its course; emaciation and loss of strength are rapid, anorexia and vomiting are extreme, the headache severe, the stools invariably clay-colored, and the portal circulation greatly impeded, leading to the development of ascites and the œdema aforementioned. Fever does not occur in uncomplicated cases of obstructive cirrhosis; the jaundice, sudden in its onset, is extreme from its first appearance, a diminution of the yellowish color of the skin and conjunctiva practically never occurring. The systemic disturbances are marked, especially the itching of the skin, with hemorrhages beneath its upper layer, and the headache and vomiting. The disease is rapidly progressive, the patients have no intermission of their characteristic symptoms, but rapidly lose strength and flesh, sinking into that condition of coma or of auto-intoxication which is only ended by death itself.

CONCLUSIONS. From the study of the cases of cirrhosis seen in Montreal, and from a review of the cases reported by other authors, together with the observations of experimental pathologists, we are justified in drawing a number of general conclusions:

Complete obstruction to the flow of bile in *animals* produces a cirrhosis of the liver, interlobular in character, of considerable extent, provided the animals are allowed to live a sufficient time after primary operation. This cirrhosis is due to the damming back of bile *per se*, and not to the inflammation of the walls of the smaller bile channels.

In *man*, complete obliteration of the bile-ducts caused by pathological changes leads to a cirrhosis of the liver which cannot be explained simply by the damming back of bile, but must be considered to have, as an added etiological factor, that inflammation of the walls of the biliary channels which is invariably present.

The type of the cirrhosis of the liver seen in man subsequent to obstruction of the bile passages cannot be differentiated anatomically from the type of liver seen in Hanot's hypertrophic cirrhosis with jaundice.

The symptom-complex of obliterative cirrhosis is so absolutely different from Hanot's cirrhosis in the variety of its symptoms and in the frequency with which they occur as to justify the statement that *obstructive biliary cirrhosis* is a distinct morbid condition quite apart from any other variety of cirrhosis of the liver.

SYMPTOM-COMPLEX OF HANOT'S CIRRHOSIS AND OBSTRUCTIVE BILIARY CIRRHOSIS.

Symptoms.	Hanot's Cirrhosis.	Obstructive Cirrhosis.
Course of disease . . .	Chronic.	Acute.
General health . . .	Good.	Poor.
Emaciation	Slow.	Rapid.
Loss of weight . . .	Slow.	Rapid.
Intermission of symptoms .	Common.	Does not occur.
Fever	Common.	Rare.
Anorexia	Rare.	Common.
Good appetite . . .	Common.	Rare.
Vomiting	Rare.	Common.
Jaundice	Slight at first, increasing.	Deep from the first.
Clay-colored stools . .	Rare.	Constant.
Bile-stained urine . .	Common.	Constant.
Enlargement of liver . .	Common.	Common.
Contraction of liver . .	Rare.	Common.
Ascites	Rare.	Common.
Œdema of extremities .	Rare.	Common.
Caput medusæ . . .	Rare.	Common.

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DORSAL DISLOCATION OF THE TRAPEZOID.

By John Glendon Sheldon, M D.,
INSTRUCTOR IN MATERIA MEDICA IN THE RUSH MEDICAL COLLEGE, CHICAGO.

Dorsal dislocation of the trapezoid, unaccompanied with fracture or dislocation of other bones, occurs so rarely that it may be looked upon as a surgical curiosity. I could find in the *Index Medicus* and in the *Index Catalogue of the Library of the Surgeon-General's Office* the report of only one case. This was recorded by Geo. W. Gay in the *Boston Medical and Surgical Journal* in 1869.

In this paper I shall give a summary of Gay's case, and shall report a case of injury that came to me and was diagnosed and treated as a case of simple uncomplicated dorsal dislocation of the trapezoid.

Dr. Gay's patient injured his wrist by striking a post in such a